EXPLANATION OF SOME FEATURES OF THE CARDIOVASCULAR CONTROL IN HORSES

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Abstrakt V EKG záznamech koní snímaných v dynamických experimentech bylo zjištěno, že při zkracování intervalů RR dochází v mnoha případech k současnému prodloužení intervalů QT. Příčiny tohoto jevu nebyly dosud vysvětleny ani veterinární, ani humánní medicínou. Z námi provedených simulačních experimentů vyplývá, že komorová aktivita srdce je řízena alespoň dvěma vlivy, z nichž jeden komorovou aktivitu stimuluje, druhý potlačuje. Hodnoty parametrů našeho modelu naznačily, že tyto vlivy mohou být jak nervového, tak hormonálního původu.

Summary Shortening of RR intervals is often associated with prolonging QT intervals in dynamic studies of the cardiovascular activity in horses. Causes of the relationship have not been explained neither in veterinary nor human medicine yet. Our simulation experiments explain that the heart ventricle activity is controlled by at least two phenomena. One of them is stimulating and the other inhibiting. The identified values of the model parameters denote that the control effects are supposed to be both nervous and humoral.

1. INTRODUCTION

Past studies on controlling the myocardium based on the cardiovascular system anatomy show that there are two mechanisms (stimulating and inhibiting) controlling performance of heart in organism. The task of our project was to describe mathematically the sympathetic (stimulating) and vagal (inhibiting) activities in a vegetative part of nervous system. Direct measurement of electrochemical activity of both branches would be very complicated considering practical reasons (invasive measurement; difficulties in connecting the measuring electrodes to the nervous fibres outside of laboratory environment etc.). Therefore, we decided to use data from indirect measurements through the activity of organs, which are controlled by the vegetative nervous system.

The anatomy of equine heart shows that open ends of vegetative nerves have a great density close to the sine node which is the basic source of electrical impulses in heart muscle and determines a heart rate. Thus sine node also determines the length of RR intervals in ECG. RR intervals can serve as an indirect indicator of common sympathetic and parasympathetic activity. In our work we assumed mutually independent activities of both branches. Two independent controlling mechanisms are fully described by two signals, therefore, we have to define another nervous activity indicator. There are open nervous ends of both vegetative branches in equine heart ventricles. That is why a suitable solution for defining another nervous activity indicator was choosing a sequence of QT intervals (time of spreading the electrical excitation through tissue of myocardium ventricles).

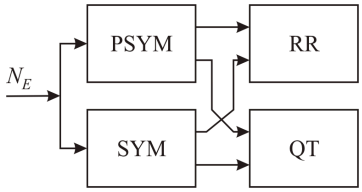

Fig. 1. Principle structure of the cardiovascular system control

Based on knowledge of the sequences of RR and QT intervals we designed a model of a myocardium control that could help to explain the causes of control mechanisms of the heart performance [4].

2. EXPERIMENTAL

Block diagram of the model structure is depicted in Fig. 1. As follows from our previous studies [1], [4] we used the formula

$$RR(t) = RR_{SAU} - k_{SR} N_S(t) + k_{PR} N_P(t) \qquad (1)$$

for generating sequences of RR intervals. RR_{SAU} is a basic heart period of sine node and N_S and N_P represent sympathetic and parasympathetic activity levels. k_{SR}, k_{PR} are multiplicative parameters that express levels of influence of each neural branch upon the duration of RR intervals. Similarly,

$$QT(t) = QT_0 - k_{SQ} N_S(t - \tau_{SQ}) + \\ + k_{PQ} N_P(t - \tau_{PQ}) \qquad (2)$$

describes an equation generating QT intervals where τ_{SQ} and τ_{PQ} are delays in sympathetic and parasympathetic neural branches in heart ventricles

and k_{SQ}, k_{PQ} are multiplicative parameters, similar to those in the eq. (1). Q_{T0} is a basic length of QT interval at neural ventricular blockade. Both the delays are connected with the finite velocity of nervous stimulation spreading.

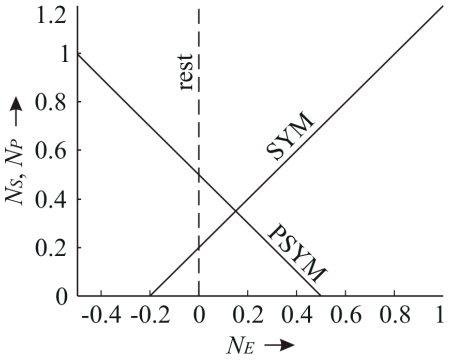

Fig. 2.: Sympathetic and/or parasympathetic sensitivities, N_S, N_P

The aim of extending the described model was to find the internal structure of the subsystems SYM and PSYM (see Fig. 1) and their mutual relationship. The models for simulating static and dynamic properties of both the types of nerves fibres have structures depicted in Fig. 3, as published in [2] and [3]. First of all, it was necessary to describe sensitivity of the fibres on their stimulation represented by input signal N_E. In our model, we have used bottom-limited piecewise linear function (Fig. 2)

$$N_{S,P} = \begin{cases} a_{S,P} N_E + b_{S,P} & \text{if } N_E > -\dfrac{b_{S,P}}{a_{S,P}} \\ 0 & \text{otherwise} \end{cases} \tag{3}$$

where indexes "*S*" and/or "*P*" represent sympathetic and parasympathetic branch, $a_{S,P}$ is the sensitivity coefficient. Inertia of the nerves is modelled by the first-order low-pass filter described by the frequency response

$$F(\mathrm{j}\omega) = \frac{k}{T_X \mathrm{j}\omega + 1} \cdot \mathrm{e}^{-\mathrm{j}\omega\tau_X} \tag{4}$$

where ω represents a frequency, T_X is a time constant of the filter, τ_X is a unit delay and k is a gain of filter. The inertia is associated with the limited delay in response of the cells to their excitation. Finally, the "time-delay" block t represents a final velocity of spreading of the excitation along nervous threads and/or heart tissue.

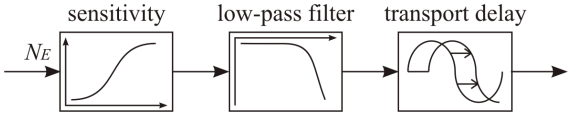

Fig. 3. Basic structure of nervous fibres' model

Input signal N_E represents response of the neural feedback to impulse stimulation. It is described as

$$N_E = \begin{cases} A.\left[\sin\left(\dfrac{2\pi}{T}(t - t_1) - \dfrac{\pi}{2}\right) + 1\right], \\ \quad \text{if } t_1 \le t \le t_1 + T \\ 0, \quad \text{otherwise,} \end{cases} \tag{5}$$

where T is a duration of the input impulse and t_1 represents its lag after some reference starting point.

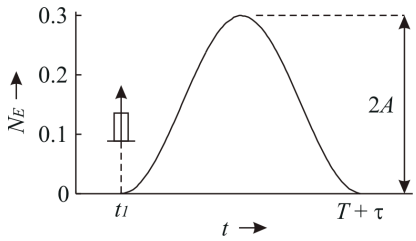

Fig. 4. Input signal N_E

Fig. 5 shows a structure of the nervous heart control. It is based on the hypothesis that QT intervals are not controlled by the nervous activity only, but we can identify an indirect dependency of QT intervals on heart rate and its variability.

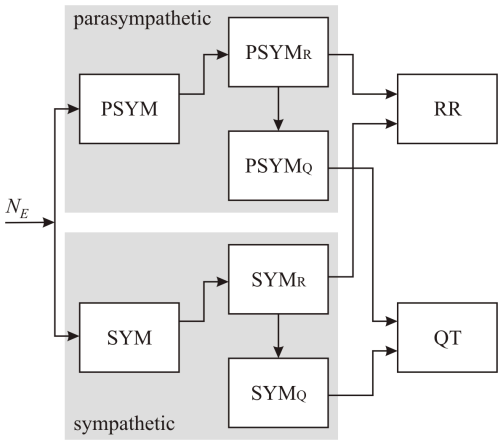

Fig. 5. Detail structure of nervous control

3. RESULTS

The simulation results have been compared to 4 most representative sets of experimental data. The criterion for choosing records was noiseless signal with considerable changes in the sequences of RR and QT intervals as responses to impulse stimulation. The aim of the work is to define properties of controlling subsystems, we have identified some of the model parametres as time constants of the filters (T_{SRp}, T_{PRp}, T_{SQp}, T_{PQp} and/or T_{SRs}, T_{PRs}, T_{SQs}, T_{PQs}), time delays (τ_{SQp}, τ_{PQp} and/or τ_{SQs}, τ_{PQs}) and gain factors (k_{SQp}, k_{PQp} and/or k_{SQs}, k_{PQs}). We used Mat-

lab® Optimization Toolbox as an optimization tool. A root mean square error between simulated and real experimental data has been used for an optimization and its minimum was searched by the gradient method. The identification results for two different types of records are summarized in Table 1:

a) direct dependency QT on RR intervals – shortening of the RR intervals is followed by the shortening of QT intervals (Figure 6a)
b) relationship between RR and QT that is not explained yet – shortening of the RR causes almost immediate *prolonging* of the sequences of QT intervals (Figure 6b).

Tab. 1. Summary of optimized parameters for two different relationships between sequences of RR and QT intervals

record 1 (velvet - s el 1 - 2002-04-24)	record 2 (nikita - s el - 2002-04-24)
$T_{SR} = 25$ s	$T_{SR} = 4$ s
$T_{PR} = 25$ s	$T_{PR} = 4$ s
$T_{SQ} = 19$ s	$T_{SQ} = 18$ s
$T_{PQ} = 17$ s	$T_{PQ} = 18$ s
$\tau_{SQ} = 18$ s	$\tau_{SQ} = 4$ s
$\tau_{PQ} = 20$ s	$\tau_{PQ} = 1.2$ s
$k_{SQ} = -5.1$	$k_{SQ} = -4.2$
$k_{PQ} = -4.6$	$k_{PQ} = -4.6$

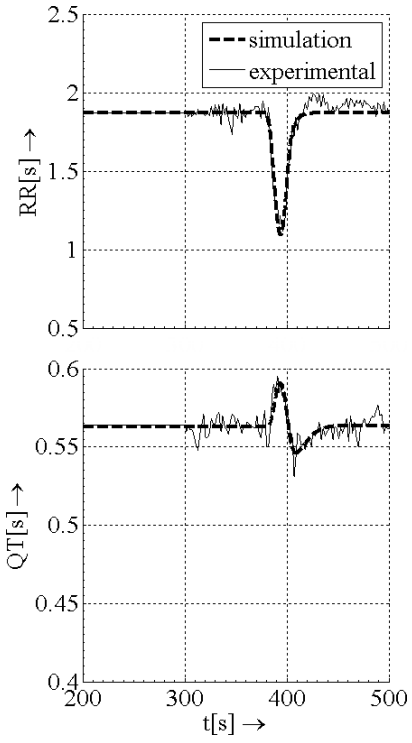

Fig. 9. Bi-phase sequences of QT intervals (heda1)

4. CONCLUSIONS

Having identified model parameters by means of computer simulations we are able to explain fundamental causes of various behaviour of the QT intervals. We recognised almost linear dependency with positive slope constant between optimum parameters of τ_{SQ}, τ_{PQ}, and T_{SQ}, T_{PQ},. It is due to the fact that the developed model uses linear subsystems only (the non-linear functions $N_S = N_S(N_E)$ and NP = NP(NE) are used in their linear parts only) and the input signal NE is used for both sympathetic and parasympathetic branch.

We have proved experimentally that the simple shape of the QT interval sequences with one local extreme is generated by the model using very similar values of τ_{SQ}, τ_{PQ} and T_{SQ}, T_{PQ} in both the neural branches. If the supposition about the similarity of the above mentioned parameters is not valid then the signals NS, NP are mutually shifted in time. The mutual shift will cause a change of the QT sequence shape. In the case, one local extreme is substituted by biphasic waveform with local maximum and minimum (Fig. 9).

Dependency of parameters k_{PQ}, k_{SQ} can be approximated well by a linear relationship with a negative slope constant (see the x-y projection of the optimum path in Fig. 7 and Fig. 8)

$$k_{SQ} = a.k_{PQ} + b, \tag{6}$$

where the estimated values of coefficients $a = -2$ and $b = -13.5$ are roughly valid for all analysed records. If we suppose the simplified criteria $\tau_{SQ} = \tau_{PQ}$ and $T_{SQ} = T_P$, then the breaking point between the direct (Fig. 6a) and inverse (Fig. 6b) dependency of QT on RR intervals is set for $k_{SQ} = k_{PQ} = -4.5$. Then for $k_{SQ} > k_{PQ}$ we observe the direct and for $k_{SQ} < k_{PQ}$ the inverse dependency of QT on RR intervals.

Acknowledgement

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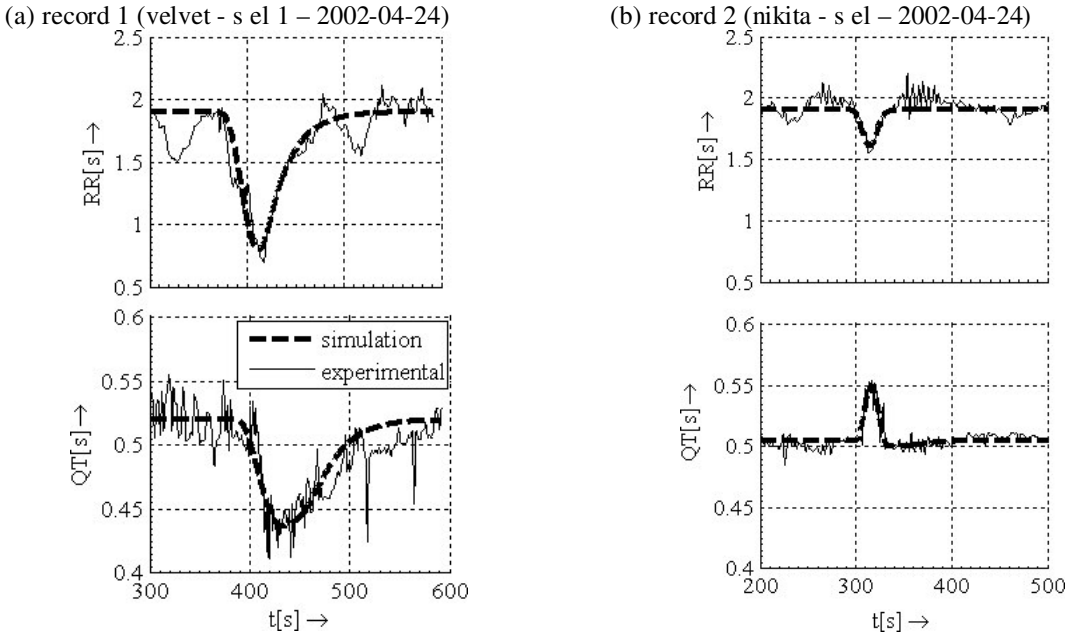

Fig. 6. Experimental and simulated data generated by the optimized parameters

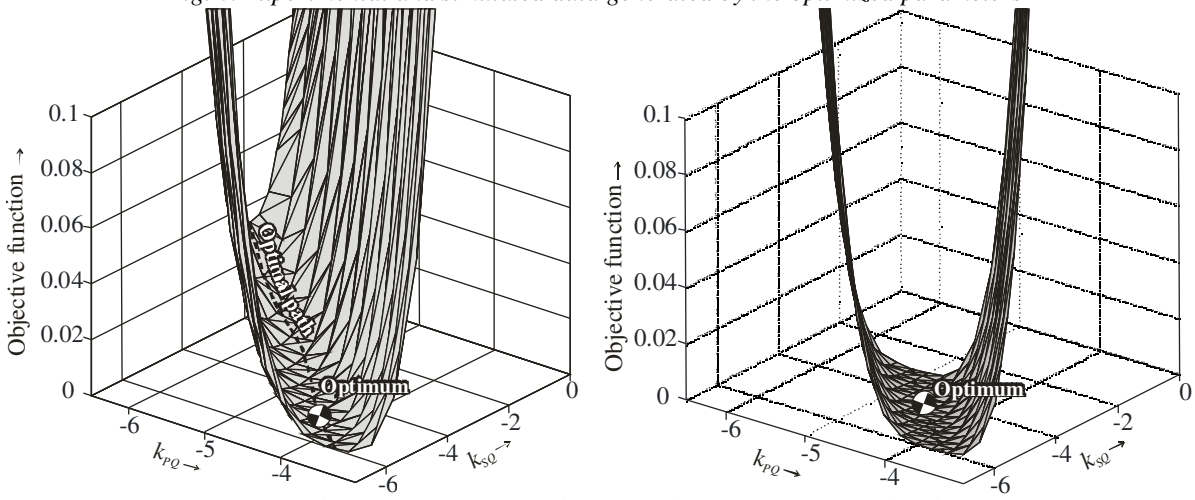

Fig. 7. Objective functions for different values of gain factors k_{SQ}, k_{PQ}.

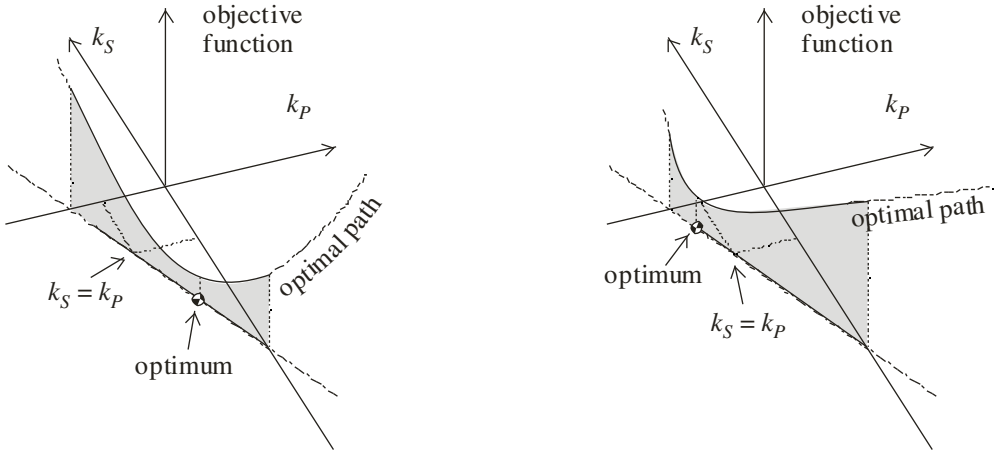

Fig. 8. Schematic explanation of different behaviour in equine heart ventricles